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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,662	08/31/2001	Nobuko Yamamoto	35.C15716	7800

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/942,662	Yamamoto et al.
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *8/31/01 and 11/21/01 and 2/10/02* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-107* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *93-106* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-92 and 107* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Aug 31, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *09/942,662* .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-44 and 64-92, drawn to method of nucleic acid hybridization, classified in class 435, subclass 6.

II. Claims 45-63, drawn to biological matrix, classified in class 345, subclass 55.

III. Claims 93-106, drawn to detection substrate, classified in class 427, subclass 7.

IV. Claim 107, drawn to method of preparation of matrix, classified in class 101, subclass 401.2.

2. The inventions are distinct, each from the other because of the following reasons: Inventions of Groups I and II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the method of nucleic acid hybridization of Group I can be practiced by the biological matrix, and detection substrate of Groups II and III respectively or can be practiced by solution based hybridization without any solid substrate or by mass spectrometry.

3. Inventions of Groups I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation,

different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of method of nucleic acid hybridization of Group I are not disclosed as capable of use together with method of preparation of matrix of Group IV and they have different modes of operation, different functions, or different effects.

4. Inventions of Groups II and III are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention has separate utility such as detection of proteins can be practiced by biological matrix of Group II whereas detection substrate of Group III can detect only oligonucleotides. See MPEP § 806.05(d).

5. Inventions of Groups II and IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product of Group II can be made by the method of Group IV or can be made by photolithography.

6. Inventions of Groups III and IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the

instant case the product of Group III can be made by the method of Group IV or can be made by photolithography.

7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

8. During a telephone conversation with Jason Okun on April 10, 2002 a provisional election was made with traverse to prosecute the invention of Group III, claims 93-106. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-92 and 107 are withdrawn from further consideration by the examiner, 37 CAR 1.142(b), as being drawn to a non-elected invention.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CAR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CAR 1.48(b) and by the fee required under 37 CAR 1.17(I).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 93, 94, 96, 97, 102, and 103 are rejected under 35 U.S.C. 102 (b) as being anticipated by Southern (European Patent Publication Number EP 0 373 203 B1) (June 20, 1990).

Southern teaches a detection substrate with two or more oligonucleotides having known base sequences different from one another fixed on a solid substrate (page 6, lines 13-27, Claims 10-18 and Examples 1-5), wherein the two or more oligonucleotides are bound and fixed on a plurality of predetermined sections by covalent bonds, respectively, so that one oligonucleotide is present in each section, and the plurality of predetermined sections with oligonucleotides fixed therein are arranged in a matrix form on a surface of the solid substrate (page 6, lines 13-27, Claims 10-18 and Examples 1-5 and page 10, lines 25-45).

Southern teaches a detection substrate wherein the known base sequence of each of the two or more oligonucleotide bound in predetermined sections has a base length of 2 to 60 (Examples 1, 3, and 5).

Southern teaches a detection substrate wherein the substrate is a glass substrate (Page 6, lines 44-49 and Examples 1, and 5).

Southern teaches a detection substrate wherein the two or more oligonucleotides are fixed in each of the predetermined sections such that one oligonucleotide is present in each section by supplying the two or more oligonucleotides in each of the predetermined sections in a matrix form by printing them by an ink-jet process (Example 5).

Southern teaches a detection substrate wherein the two or more oligonucleotides are bound to the plurality of predetermined sections previously partitioned in a matrix form (page 6, lines 13-27, Claims 10-18 and Examples 1-5 and page 10, lines 25-45).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 93- 97, 102, and 103 are rejected under 35 U.S.C. 103 (a) over Southern (European Patent Publication Number EP 0 373 203 B1) (June 20, 1990).

Southern teaches the detection substrate of claims 93, 94, 96, 97, 102, and 103 as described above.

Southern does not teach the detection substrate, wherein the plurality of predetermined sections are arranged in a matrix form on the surface of the solid substrate at a density of 400/ square cm or lower.

However, it is *prima facie* obvious that selection of the specific density of plurality of predetermined sections represent routine optimization with regard to sequence, length and compositions of the DNA sequences being screened as well as the size and sequence of the capture molecule and the requirement of screening speed which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of the specific density of plurality of predetermined sections performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

14. Claims 93- 99, 102, and 103 are rejected under 35 U.S.C. 103 (a) over Southern (European Patent Publication Number EP 0 373 203 B1) (June 20, 1990) in view of Chrisey et al. (U.S. Patent 5,688,642) (November 18, 1997).

Southern teaches the detection substrate of claims 93- 97, 102, and 103 as described above.

Southern does not teach the detection substrate, wherein the oligonucleotides are fixed on the detection substrate by covalent bonds formed through a chemical reaction of maleimide groups introduced to a glass surface of the solid substrate with thiol groups possessed by the oligonucleotides.

Chrisey et al. teach the detection substrate, wherein the oligonucleotides are fixed on the detection substrate by covalent bonds formed through a chemical reaction of maleimide groups introduced to a glass surface of the solid substrate with thiol groups possessed by the oligonucleotides (Abstract and Column 7, line 65 to column 8, line 12).

Southern does not teach the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting succinimidyl 4-(maleimidophenyl) butyrate with the amino groups.

Chrisey et al. teach the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting succinimidyl 4-(maleimidophenyl) butyrate with the amino groups (Column 7, line 65 to column 8, line 12).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass

surface and then reacting succinimidyl 4-(maleimidophenyl) butyrate with the amino groups of Chrisey et al in the detection substrate of Southern, since Chrisey et al. state, "A heterobifunctional crosslinker found useful for the covalent attachment of a thiol-modified synthetic DNA to an aminosilane-modified substrate was succinimidyl 4-(maleimidophenyl) butyrate (SMPB), which has an amino reactive succinimide ester and a thiol group reactive maleimide group (Column 8, lines 8-13)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting succinimidyl 4-(maleimidophenyl) butyrate with the amino groups of Chrisey et al in the detection substrate of Southern in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Chrisey et al., of succinimidyl 4-(maleimidophenyl) butyrate (SMPB), which is a heterobifunctional crosslinker found useful for the covalent attachment of a thiol-modified synthetic DNA to an aminosilane-modified substrate.

15. Claims 93-100, 102, and 103 are rejected under 35 U.S.C. 103 (a) over Southern (European Patent Publication Number EP 0 373 203 B1) (June 20, 1990) in view of Chrisey et al. (U.S. Patent 5,688,642) (November 18, 1997) further in view of Sakaki et al. (U.S. Patent 5,807,942) (September 15, 1998).

Southern in view of Chrisey et al. teach the detection substrate of claims 93- 97, 102, and 103 as described above.

Southern in view of Chrisey et al. do not teach the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting N-(6-maleimidocaproyloxy) succinimide with the amino groups.

Sakaki et al. teach the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting N-(6-maleimidocaproyloxy) succinimide with the amino groups (Example 1-1, Example 6-1, and Example 11-2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting N-(6-maleimidocaproyloxy) succinimide with the amino groups of Sakai et al in the detection substrate of Southern in view of Chrisey et al., since Sakaki et al. state, "By the reaction of the free amino group in the Bioprase with the succinimidyloxycarbonyl group in the modifying agent, the modifying agent was introduced into Bioprase through amido bonds (Column 16, lines 20-23)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the detection substrate, wherein the maleimide groups introduced to the glass surface are formed by first introducing amino groups to

the glass surface and then reacting N-(6-maleimidocaproyloxy) succinimide with the amino groups of Sakaki et al in the detection substrate of Southern in view of Chrisey et al. in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Sakaki et al., of N-(6-maleimidocaproyloxy) succinimide, by which the desired modifying agent can be introduced into the substrate of choice through amido bonds.

16. Claims 93- 97, and 101-103 are rejected under 35 U.S.C. 103 (a) over Southern (European Patent Publication Number EP 0 373 203 B1) (June 20, 1990) in view of Eggers et al. (U.S. Patent 5,891,630) (April 6,1999).

Southern teaches the detection substrate of claims 93- 97, 102, and 103 as described above.

Southern does not teach the detection substrate, wherein the oligonucleotides are fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass surface of the solid substrate with amino groups possessed by the oligonucleotides.

Eggers et al. teach the detection substrate, wherein the oligonucleotides are fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass surface of the solid substrate with amino groups possessed by the oligonucleotides. (column 8, lines 5-13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the detection substrate, wherein the

oligonucleotides are fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass surface of the solid substrate with amino groups possessed by the oligonucleotides of Eggers et al in the detection substrate of Southern, since Eggers et al. state, "The solid support substrates must be functionalized to create a surface chemistry conducive to the formation of covalent linkages with the selected probes (Column 8, lines 5-8)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the detection substrate, wherein the oligonucleotides are fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass surface of the solid substrate with amino groups possessed by the oligonucleotides of Eggers et al in the detection substrate of Southern in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Eggers et al., of an invention which provides the creation of a surface chemistry conducive to the formation of covalent linkages with the selected probes.

17. Claims 93- 97, and 102-106 are rejected under 35 U.S.C. 103 (a) over Southern (European Patent Publication Number EP 0 373 203 B1) (June 20, 1990) in view of Gordon et al. (U.S. Patent 5,601,980) (February 11, 1997).

Southern teaches the detection substrate of claims 93- 97, 102, and 103 as described above. Southern also teaches the detection substrate, wherein the wall member has a thickness in the range of 1 to 20 micrometer (Page 6, lines 44-46).

Southern does not teach the detection substrate, wherein each section of the matrix has a hydrophobic wall portion and a hydrophillic bottom portion.

Gordon et al. teach the detection substrate, wherein each section of the matrix has a hydrophobic wall portion and a hydrophillic bottom portion (Column 4, line 43 to Column 5, line 24).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the detection substrate, wherein each section of the matrix has a hydrophobic wall portion and a hydrophillic bottom portion of Gordon et al in the detection substrate of Southern, since Gordon et al. state, "The indices may also be provided with a hydrophobic coating to prevent undesired traveling of the probe to an adjacent cell (Column 4, lines 52-54)." Gordon et al further state, "Once the droplet contacts the hydrophilic surface of the cell, the droplet wicks completely onto the cell (Column 5, lines 19-21 and Fig. 2C)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the detection substrate, wherein each section of the matrix has a hydrophobic wall portion and a hydrophillic bottom portion of Gordon et al in the detection substrate of Southern, in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Gordon et al., of the hydrophobic coating of the wall of matrix portions to prevent undesired traveling of the probe to an adjacent cell and the hydrophilic bottom so that the test substance or the probe wicks completely onto the cell.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

April 12, 2002

W. Gary Jones
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